

Attorney Docket No: 16517  
Application No. 10/775,176  
Page 6 of 9

## REMARKS

### Objection to the Title

The title has been amended to describe the invention to which the claims are directed. The amendment to the title is supported throughout the Abstract and Specification, including, for example:

"...invention relates to the probabilistic analysis of nucleic acid sequences for the determination of coding features, including..." (page 73, lines 2 – 3, and page 3, lines 24 – 25)

"Described herein are methods, devices, and systems for analyzing the information content in nucleic acids." (page 3, lines 28 – 29)

These "coding features" or "information content" are described as

"...strand coding..." (page 4, line 26, and figure 3),

"extent of open reading frame" (page 5, lines 10 – 11, and figure 4),

"locations of insertions and deletions" (page 4, lines 18 – 19, and figure 5), and

"exon location" (page 6, line 4, and figure 6).

This method provides for these coding features as a statistically probable state for each examined nucleotide in a nucleic acid sequence (e. g., Example 3, pages 48 through 61).

### Rejection under 35 U.S.C. 101

Examiner rejects claims 52, 56-57, and 60 alleging that "the claimed Invention is directed to non-statutory subject matter". While Examiner admits this invention produces "a concrete and useful result", Examiner points out, "there is no tangible result." Applicant thanks the Examiner for her suggestion that "amending the claims to recite a step of outputting the result or a physical transformation, would nullify this rejection". Applicant adds a step f) in claim 52 to recite a step that provides said nucleic acid sequence as a sequence of most probable states; it is this sequence of most probable states that demarcates the coding features, which in turn define the coding product, a protein sequence. Amendment of claim 52 to recite this step is supported by the specification, for example:

"...process begins by determining the state probabilities for each nucleotide in the nucleic acid sequence, the coding strand, and the extent of the open reading frame. The process then classifies each nucleotide according to its most probably state. Filters, which reclassify nucleotides in a defined manner in order to make local blocks of the nucleic acid sequence consistent, are then applied to the nucleic acid

Attorney Docket No: 16517

Application No. 10/775,176

Page 7 of 9

sequence. Regions of the nucleic acid sequence that are in any of classes 1, 2, or 3 are then designated as exons, and the exons are translated. Translation is accomplished by using the universal genetic code to convert the nucleic acid sequence of the designated exons into the corresponding amino acid sequence based on the reading frame of the class. That is, exons in class 1 will be translated in reading frame 1, exons in class two will be translated in reading frame 2, and exons in class 3 will be translated in reading frame 3. The translation is linearly arranged to correspond to the linear arrangement of the exons along the nucleic acid sequence." (page 32, line 30 to page 33, line 11)

Applicants respectfully request entry of this amendment, which also obviates the rejection of claims 56, 57, and 60, which depend from claim 52.

**Rejections under 35 U.S.C. 112, First Paragraph (written description)**

Examiner rejects claims 52, 56-57, and 60 alleging that the introduced term "selected" is not supported in the specification. Applicant has amended the claims to recite the term "examined" in place of the term "selected", as fully supported by the specification:

"In order to determine the state probabilities for more than one nucleotide, a window is used for each nucleotide that is **examined**. The nucleotide that is being **examined** is within the window, and the probability determinations set out in equations I, II, III, and IV are performed for the sequence in the window. The oligonucleotide probabilities are determined as before for the nucleic acid sequence in the window. The oligonucleotide probabilities for each of the states are determined for the nucleic acid sequence within the window, and those probabilities are assigned to the nucleotide within the window state probabilities are being determined, which, in a preferred embodiment, is the middle nucleotide. Another nucleotide is then **examined**, with the window shifted or redefined around the new nucleotide, and so on, until the final nucleotide in the nucleic acid sequence for which state probabilities are to be determined is reached." (page 25, line 22 to page 26, line 4 with emphasis added)

Examiner rejects claims 52, 56-57, and 60 alleging that the introduced phrase, "the value produced by said bias function", when interpreted literally, has a meaning not supported by the specification. The Examiner points out that the phrase, "the value produced by said bias function", interpreted correctly, does not mean what Applicant intends, which is the value "being used in" the bias function. Applicant has amended claims 52 and 60 to recite "being used in" rather than "produced by", thus placing these claims in condition for allowance.

Attorney Docket No: 16517  
 Application No. 10/775,176  
 Page 8 of 9

Examiner is not convinced that the equation in Claim 52 of  $P(f | s)$  with " $\Phi(i)$ " is adequately supported by the specification. Applicant amends claim 52 to recite equation XXXI from the specification on page 46:

$$P'(\sigma | S) = \frac{\phi(\sigma) \cdot P(\sigma) \cdot P(S | \sigma)}{\sum_i [\phi(i) \cdot P(i) \cdot P(S | i)]}$$

Equation XXXI is used in EXAMPLE 2 where

"initial probabilities are all 1 and each event is independent of that which precedes it ( $a_1, \dots, a_k \rightarrow a_{k+1}$ , becomes  $N \rightarrow a_1$ , because  $k$  is zero)."

Equation XXXI clearly shows that the product of each operand under summation in the denominator will be at least different in at least one state from the other states because the value being used in the bias function  $\phi(i)$  is different in at least one state from the other states.

#### **Rejections under 35 U.S.C. 112, First Paragraph (Enablement)**

The Examiner points out that the equation in previously amended claim 52 is not identical to equation IV on page 24 of the Specification and alleges that "the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims." Applicant points out that the working Examples in the specification illustrate reduction to practice. For instance, EXAMPLE 2 uses hypothetical initial probabilities to demonstrate a clear and simple method of using the invention and thereby enabling it. The amendment of claim 52 to recite equation XXXI is made because equation XXXI provides guidance as to how equation IV is to be used. Amended claim 52 incorporates equation XXXI from the Specification page 46 and nullifies this rejection.

#### **Rejections under 35 U.S.C. 112, Second Paragraph (Indefiniteness)**

The Examiner rejects claim 52 because, "The preamble of claim 52 is directed to method for gene prediction..." and the body, "does not recite any gene prediction." The preamble of claim 52 is amended to more clearly recite the result of this method, i. e., "A method for

Attorney Docket No: 16517  
Application No. 10/775,176  
Page 9 of 9

determining coding features within a nucleic acid sequence..." Claim 52 is additionally clarified by reciting additional step f); this clarification is also reflected in the amendment to the title.

The Examiner points out an error by the applicant that "the value", which occurs in claim 52 and 60, lacks antecedent basis. Claim 52 is amended to read, "a value", providing proper antecedent basis to the "the value" in claim 60.

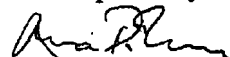
The Examiner alleges that the phrase, "is at least different in one state within all of said states" is unclear. Claim 52 is amended for clarity to recite that "a value is different in [at least] one state from the other states".

The Examiner suggests "a listing of exact definitions of [the] terms [in the equation] in claim 52". The claim has been amended for clarity to include this list of exact definitions.

#### Summary

In view of the above amendments addressing specific rejections and objections, Applicant urges the Examiner to reconsider removing the finality of this office Action and indicate allowance of the amended claims. If the Examiner has any questions regarding this application, the Examiner is encouraged to contact Applicants' undersigned agent at (860) 572-5217 (telephone) or (860) 572-5280 (fax).

Respectfully submitted,



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